Claims

Sub C7

1. A method for stimulating an immune response specific toward a naturally-occurring protein in an animal having an immune system including T cells, said method comprising administering to said animal an altered protein or polypeptide fragment thereof derived from said naturally-occurring protein, wherein an unstable polypeptide segment has been inserted by artifice into said altered protein.

2. The method of claim 1, wherein said naturally-occurring protein is from a pathogen.

3. The method of claim 2, wherein said altered protein or polypeptide fragment thereof is administered to said animal to prevent infection of said animal with said pathogen.

4. The method of claim 1, wherein said naturally-occurring protein is from a neoplastic cell,

5. The method of claim 4, wherein said altered protein or polypeptide fragment thereof is administered to said animal to inhibit growth of said neoplastic cell in said animal.

6. The method of claim 1, wherein said altered protein or polypeptide fragment thereof is administered with a pharmaceutically acceptable carrier, an adjuvant or both.

7. The method of claim 1, wherein said animal is a mammal.

8. The method of claim 7, wherein said mammal is a human.

Sub B1

9. A method for increasing the immunogenicity of a naturally-occurring protein, said method comprising inserting by artifice into said naturally-occurring protein an unstable polypeptide segment to produce an altered protein.

10. The method of claim 9, wherein said altered protein or polypeptide fragment thereof is in a vaccine.

Sub C8

11. The method of claim 1 or 9, wherein said unstable polypeptide segment comprises at least twelve amino acid residues.

12. The method of claim 11, wherein not more than 30% of said amino acid residues are selected from the group of amino acid residues consisting of isoleucine, leucine, valine, tyrosine, phenylalanine, tryptophan, threonine, and methionine.

Sub C9

13. The method of claim 1 or 9, wherein said unstable polypeptide segment comprises a polypeptide sequence that is specifically recognized by a protease.

14. The method of claim 1 or 9, wherein said unstable polypeptide segment has an average hydrophobicity value that is lower than the average hydrophobicity value of said altered protein; has a sequence conservation that is lower than a sequence conservation of said altered protein; has an amide protection factor that is lower than 10^4 wherein said altered protein is in a native conformational state; has an average amide protection factor that is lower than the average amide protection factor for said altered protein in a denatured conformational state; has an NMR order parameter (S^2) of less than 0.8; or has an average B-factor value that is higher than the average B-factor value of said altered protein.

Sub C10

15. The method of claim 1 or 9, wherein said altered protein comprises a T cell epitope.

16. The method of claim 15, wherein said unstable polypeptide segment is inserted N-terminally adjacent to said T cell epitope.

17. The method of claim 15, wherein the C - terminal portion of said unstable polypeptide segment overlaps the N - terminal portion of said T cell epitope.

18. The method of claim 15, wherein said T cell epitope has an average hydrophobicity value that is higher than the average hydrophobicity value of said altered protein; has a sequence conservation that is higher than a sequence conservation of said altered protein; has an amide protection factor that is greater than 10^4 wherein said altered protein is in a native conformational state; has an average amide protection factor that is higher than the average amide protection factor for said altered protein in a denatured conformational state; has an NMR order parameter (S^2) of greater than 0.7; or has an average B-factor value that is lower than the average B-factor value of said altered protein.

19. The method of claim 15, wherein at least 30% of the amino acid residues of said T cell epitope are selected from the group of amino acid residues consisting of isoleucine, leucine, valine, tyrosine, phenylalanine, tryptophan, threonine, and methionine.

20. A method for detecting in a substantially pure protein a polypeptide segment that is likely to be a T-cell epitope, said method comprising the steps of:

(a) identifying an unstable polypeptide segment in said protein; and

(b) identifying a second polypeptide segment adjacent to said unstable polypeptide segment in said protein, said second polypeptide segment likely to be a T cell epitope.

21. The method of claim 20, wherein said unstable polypeptide segment

comprises at least twelve amino acid residues.

22. The method of claim 21, wherein not more than 30% of said amino acid residues are selected from the group of amino acid residues consisting of isoleucine, leucine, valine, tyrosine, phenylalanine, tryptophan, threonine, and methionine.

23. The method of claim 20, wherein said unstable polypeptide segment comprises a polypeptide sequence that is specifically recognized by a protease.

24. The method of claim 20, wherein said unstable polypeptide segment has an average hydrophobicity value that is lower than the average hydrophobicity value of said protein; has a sequence conservation that is lower than a sequence conservation of said protein; has an amide protection factor that is lower than 10^4 wherein said protein is in a native conformational state; has an average amide protection factor that is lower than the average amide protection factor for said protein in a denatured conformational state; has an NMR order parameter (S^2) of less than 0.8; or has an average B-factor value that is higher than the average B-factor value of said protein.

25. The method of claim 20, wherein said unstable polypeptide segment is N-terminally adjacent to said second polypeptide segment.

26. The method of claim 20, wherein the C - terminal portion of said unstable polypeptide segment overlaps the N - terminal portion of said second polypeptide segment.

27. The method of claim 20, wherein said second polypeptide segment has an average hydrophobicity value that is higher than the average hydrophobicity value of said protein; has a sequence conservation that is higher than a sequence conservation

of said protein; has an amide protection factor that is greater than 10^4 wherein said protein is in a native conformational state; has an average amide protection factor that is higher than the average amide protection factor for said protein in a denatured conformational state; has an NMR order parameter (S^2) of greater than 0.7; or has an average B-factor value that is lower than the average B-factor value of said protein.

28. The method of claim 20, wherein at least 30% of the amino acid residues of said second polypeptide segment are selected from the group of amino acid residues consisting of isoleucine, leucine, valine, tyrosine, phenylalanine, tryptophan, threonine, and methionine.

29. A method for identifying the most immunogenic protein in a group of proteins, said method comprising identifying the protein comprising the most unstable polypeptide segment in said group of proteins, wherein said identified protein is the most immunogenic protein in said group of proteins.

30. The method of claim 29, wherein said most immunogenic protein is substantially purified and said group of proteins is from a neoplastic cell, a pathogen, a foodstuff, an allergen, or a tissue targeted in an autoimmune disease.

31. The method of claim 29, wherein said unstable polypeptide segment comprises at least twelve amino acid residues.

32. The method of claim 31, wherein not more than 30% of said amino acid residues are selected from the group of amino acid residues consisting of isoleucine, leucine, valine, tyrosine, phenylalanine, tryptophan, threonine, and methionine.

33. The method of claim 29, wherein said most unstable polypeptide segment has the lowest average hydrophobicity value of any unstable polypeptides segments

of said group of proteins; has the lowest sequence conservation of any unstable polypeptide segment of said group of proteins; has the lowest average amide protection factor of any unstable polypeptide segment of said group of proteins wherein said proteins in said group are in a native conformational state; has the lowest average amide protection factor of any unstable polypeptide segment of said proteins wherein said proteins in said group are in a denatured conformational state; has the lowest NMR order parameter (S^2) of any unstable polypeptide segment of said group of proteins; or has the average highest B-factor value of any unstable polypeptide segment of said group of proteins.

34. The method of claim 29, wherein said protein comprises a T cell epitope.

35. The method of claim 34, wherein said most unstable polypeptide segment is N-terminally adjacent to said T cell epitope.

36. The method of claim 34, wherein the C - terminal portion of said most unstable polypeptide segment overlaps the N - terminal portion of said T cell epitope.

37. The method of claim 34, wherein said T cell epitope has an average hydrophobicity value that is higher than the average hydrophobicity value of said protein; has a sequence conservation that is higher than a sequence conservation of said protein; has an amide protection factor that is greater than 10^4 wherein said protein is in a native conformational state; has an average amide protection factor that is higher than the average amide protection factor for said protein in a denatured conformational state; has an NMR order parameter (S^2) of greater than 0.7; or has an average B-factor value that is lower than the average B-factor value of said protein.

38. The method of claim 34, wherein at least 30% of the amino acid residues of said T cell epitope are selected from the group of amino acid residues consisting of

isoleucine, leucine, valine, tyrosine, phenylalanine, tryptophan, threonine, and methionine.

39. A method for treating an animal that has or is at risk for developing an allergic response, said method comprising administering to said animal a protein or polypeptide fragment thereof from an allergen, wherein said protein or polypeptide fragment thereof is identified as comprising the most unstable polypeptide segment in a group of proteins of said allergen.

40. A method for treating an animal that has or is at risk for developing an autoimmune disease, said method comprising administering to said animal a protein or polypeptide fragment thereof from a tissue targeted in said immune disease wherein said protein or polypeptide fragment thereof is identified as comprising the most unstable polypeptide segment in a group of proteins of said tissue targeted in said autoimmune disease.

41. The method of claim 39 or 40, wherein said protein or polypeptide fragment thereof is in a tolerogen.

42. The method of claim 39 or 40, wherein said protein or polypeptide fragment thereof is administered orally or wherein said protein or polypeptide fragment thereof is administered with a pharmaceutically acceptable carrier.

43. The method of claim 39 or 40, wherein said animal is a mammal.

44. The method of claim 43, wherein said mammal is a human.

45. A substantially pure antigen comprising an unstable polypeptide segment inserted by artifice.

46. The antigen of claim 45, wherein said unstable polypeptide segment comprises at least twelve amino acid residues.

47. The antigen of claim 46, wherein not more than 30% of said amino acid residues are selected from the group of amino acid residues consisting of isoleucine, leucine, valine, tyrosine, phenylalanine, tryptophan, threonine, and methionine.

48. The antigen of claim 45, wherein said unstable polypeptide segment comprises a polypeptide sequence that is specifically recognized by a protease.

49. The antigen of claim 45, wherein said unstable polypeptide segment has an average hydrophobicity value that is lower than the average hydrophobicity value of said substantially pure antigen; has a sequence conservation that is lower than a sequence conservation of said substantially pure antigen; has an amide protection factor that is lower than 10^4 wherein said substantially pure antigen is in a native conformational state; has an average amide protection factor that is lower than the average amide protection factor for said substantially pure antigen in a denatured conformational state; has an NMR order parameter (S^2) of less than 0.8; or has an average B-factor value that is higher than the average B-factor value of said substantially pure antigen.

50. The antigen of claim 45, wherein said substantially pure antigen comprises a T cell epitope.

51. The antigen of claim 50, wherein said unstable polypeptide segment is inserted N-terminally adjacent to said T cell epitope.

52. The antigen of claim 50, wherein the C - terminal portion of said unstable polypeptide segment overlaps the N - terminal portion of said T cell epitope.

53. The antigen of claim 50, wherein said T cell epitope has an average hydrophobicity value that is higher than the average hydrophobicity value of said antigen; has a sequence conservation that is higher than a sequence conservation of said antigen; has an amide protection factor that is greater than 10^4 wherein said antigen is in a native conformational state; has an average amide protection factor that is higher than the average amide protection factor for said antigen in a denatured conformational state; has an NMR order parameter (S^2) of greater than 0.7; or has an average B-factor value that is lower than the average B-factor value of said antigen.

54. The antigen of claim 50, wherein at least 30% of the amino acid residues of said T cell epitope are selected from the group of amino acid residues consisting of isoleucine, leucine, valine, tyrosine, phenylalanine, tryptophan, threonine, and methionine.

55. The antigen of claim 45, wherein said antigen is associated with a pharmaceutically acceptable carrier, an adjuvant, or both.

56. A vaccine comprising the antigen of claim 45.

57. A tolerogen comprising the antigen of claim 45.

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